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台灣之妊娠高血壓

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PIH in Taiwan

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Foreword

After a short delay of two months, " The 1998 Annual Report of the Taiwan society of perinatology " has finalized, now in its 6th edition of the annual report series.

Previous editions of the series had been highlighted on the topics of congenital anomalies, prenatal care, multiple pregnancy, cesarean section and preterm birth.

This year, we focused on current management of pregnancy-induced hypertension (PIH) in Taiwan.

We have incorporated data of recent developments, management of PIH in a comprehensive manner of a dozen of representative medical centers & hospitals throughtout this island. The incidence, management, maternal complications, as well as perinatal events are thoroughly discussed in this report.

I hope that this report will be a useful resource for our colleague perinatologist and for the government officials of Health Department.

We are not without tensions in our field. Next year, at virtually the end of the twentieth century, is witness a surge of knowledge and interest in every fields of medicine.

I am looking forward to the continued strength & efforts as the major force in the health care for the mother and their baby.

I wish to acknowledge our colleagues – J.H.Hung; M.Li Yang, W.H.Chen, T.T.Hsieh, and our mentors – professor Fon-Jou Hsieh, His-Yao Chen, Heung-Tat Ng. Special thanks to Drs. Cheng-Li Chen & Yvonne Cheng. Each of these scholars provide me with guidance, wisdom, and support, without their helps this work will not be possible.

My colleagues and I have worked to bring you to a particularly special report. We welcome you have it.

Chang Sheng Yin
President
Taiwan Society of Perinatology
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引 言

今年周產期醫學會白皮書終於定稿，這是白皮書系列的第六集，我們很高興連續前面五集的精神持續的為台灣周產期醫學貢獻一己之力。

今年我們著重在妊娠高血壓，我們收集了全台灣有代表性的醫學中心及醫院，將大家的研究及診治經驗綜合起來作一個精要的分析及討論，並找出今後的診治方向，希望這些資料對周產期醫學會有關的工作同仁及衛生主管機關均有參考的價值，在工作及政策上作一正確的判斷。

在二十世紀末，醫學界突飛猛進，周產期醫學亦不例外，我們將一本以往的精神持續堅持下去，也希望大家也一齊進步。非常感謝洪正修，楊勉力主任，本文由榮總婦產部陳晟立醫師負責完稿，英文部份由芝加哥大學婦產科醫師鄭雅文完成，另外陳惟華秘書長的協助，謝燦堂主任指導及我們的老師謝豐舟教授，陳晢堯教授，吳香達教授的鼓勵，這是本好書希望大家能好好的參考。

中華民國周產期醫學會

理事長　　尹　長　生

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PIH in Taiwan

INTRODUCTION

Pregnancy induced hypertension (PIH) is a disease process which only occurs in humans, and it is also the most common pregnancy induced complication. Together, postpartum hemorrhage, infection, and PIH represent the three major causes of morbidity and mortality in pregnant women, with PIH being responsible for 13.7% of maternal death[1]. In the United States, PIH is the second most common cause of maternal death, ranking only behind postpartum hemorrhage[2]. Just as death due to postpartum hemorrhage and infections have gradually declined in Taiwan, the percentage of PIH-related mortality has proportionally increased. From 1974 to 1985, PIH has been implicated as the cause of death in 23.7%[3] of all cases, only after postpartum hemorrhage's 42.4%.

Unfortunately, the cause of PIH remains unclear to date. Currently, the more acceptable concept suggests that PIH may be related to maternal immune system or other unknown factors during early pregnancy which prevented the invasion of trophoblasts to the uterus[4]. Because of the high recurrence rate of PIH in subsequent pregnancies, there are also speculations that PIH may be closely related to other hereditary factors. Indeed, PIH has been linked with a few genetic elements, including HLA-DR4[5], Angiotensinogen genes[6], or even mitochondrial DNA[7]; they all have been implicated to play a role in the pathogenesis of PIH. Thus, these theories seem to suggest that the occurrence of PIH may be determined at the moment when the sperm penetrates the egg.

Besides the immune system and the hereditary components, there are other contributing factors which may influence the development of PIH. These associated conditions include: maternal age, parity, race[8, 9], social habit (e.g. smoking), nutritional status[10], and hormonal levels[11]. Consequently, the prevalence of PIH differs significantly among each groups, ranging from 3% to 10%[12]. If not taking these components into consideration, PIH occurs in about 5% of all pregnancies. However, in Taiwan itself, the reported frequency of PIH actually varies quite significantly. According to the statistics published by Chang-Hua Christian Hospital, the incidences of PIH ranging from 9.4%[13] to 1.8% all have been published at various time periods. Due to the lack of well-established reports of PIH studied at a larger scale in Taiwan in recent years, we have collected data from 14 medical centers during 1993 to 1997. Cases of PIH occurred during this period have been examined and analyzed, in hope to obtain a clearer insight and to gain a better understanding of PIH within the recent five years in Taiwan.

DISEASE PATHOLOGY

FREQUENCY

Pregnancy induced hypertension, or PIH, is a nonspecific description of hypertension that occurs during pregnancy. It encompasses both hypertension that is newly diagnosed during pregnancy, and the further elevated blood pressures in a pre-existing hypertensive pregnant woman. Thus, PIH can be further differentiated into transient hypertension, chronic hypertension superimposed preeclampsia, preeclampsia, and eclampsia. In this study, which involves 14 medical centers located in northern, southern, eastern and western regions of Taiwan plus Hua-Lien, a total of 206,551 deliveries occurred during the five-year period, and a frequency of 2.3% was observed for PIH. Of these, transient hypertension and chronic hypertension superimposed preeclampsia incorporated 650 cases, whose disease frequencies were 0.4% and 0.14%, respectively. Excluding the above cases, preeclampsia has occurred with a frequency of 2.06%, a significantly lowered incident rate in comparison to the reported 5% in other nations. Further breakdown showed that PIH has occurred at 2% in medical centers located in the northern part of Taiwan. Central Taiwan has a frequency of 3.2%, southern regions, 2.8%, and east/Hua-Lien area (Buddist Tzuchi General Hospital) has a frequency of 2.3%. The higher proportion observed in central Taiwan may be related to or affected by the number of hospitals available in the region and the number of transferred patients to the area.

Of the patients with preeclampsia, the majorities (58.9%) are diagnosed with mild preeclampsia while severe preeclampsia make up another 38.4% and 2% with HELLP syndrome. All of the above eclamptic patients make up 2.7% of the PIH cases. And if these frequencies were calculated with respect to the total deliveries, mild preeclampsia occurs with a frequency of 1.1% and severe preeclampsia with 0.7%. The probability of developing HELLP syndrome is 0.4/1000 and eclampsia, 0.5/1000. According to data published by Chang-Hua Christian Hospital in 1986, eclampsia has an incidence rate of 0.15/1000. And of the preeclampsia patients, the likelihood of the disease progressing to HELLP syndrome is 11%. However, from 1972 to 1981, the prevalence of eclampsia has gradually declined from its peak at 4/1000 in 1974 to 1/1000 in 1981 in Taiwan. In comparison to the statistics published for England, the frequencies of eclampsia has also diminished significantly in years, from 7.4/1000 in 1930 to 0.49/1000 in 1994[14]. Interestingly, it has been observed that the prevalence of PIH is higher in developing countries: Pakistan 2.14%[15] and Turkey 7.71%[16]. Since the risk factors for eclampsia involves both maternal age and the lack of prenatal care[17], the fact that the frequency of eclampsia is at a decline indirectly but evidently reflects the advancement of

perinatal care in Taiwan in recent years.

THE RELATIONSHIP BETWEEN PIH AND AGE, PARITY

Pregnancy induced hypertension tends to occur in women with advanced maternal age and during first pregnancy. In 1986, Spellacy reported that the frequency of PIH in pregnant women age forty and higher is three times higher than that for those between 20 to 30 years-old. And Loung in 1979[18] and Sibai and colleague in 1995[19] all have indicated that PIH is much more frequent in primigravid women, as high as 60% of the PIH patients are women pregnant for the first time. The assessment of PIH risk factors by multivariable analysis indicates that both advanced maternal age (AMA) and primigravid are considered high-risk groups. Yet, it is interesting to point out that the majority of AMA patients have been pregnant more than once. Thus, for these women the probability of having PIH is still 2.7 times higher than that for younger patients[20].

According to the survey, of the patients with PIH, 55.4% of them are 30 years or older, and 23.1% of them are age 35 and above. On the other hand, primigravid women make up 55.8% of the PIH cases, in contrast to the 8.1% for patients pregnant for the fourth time or more. From the statistics published by the Women and Children Health Bureau in 1999, pregnant women age greater than 30 represent 30% of all pregnancies in 1997 while age 35 and more make up only 6.2%. Also, primigravid women composed of 42.39% of PIH patients and multiparous pregnancies (history of three or more deliveries) accounted for only 4% of the PIH cases. Clearly, PIH, maternal age, and parity are intricately associated with one another. To further analyze PIH by its degree of severity, it is divided into subcategories. In mild preeclamptic patients, those 35 and older represent 18.5% in contrast to patients pregnant for the first time making up 67.3%. For HELLP patients, those 35 and older make up 19.2% and the primagravid women represent 44.6%. And for severe preeclamptic patients, 24.4% of them are age 35 or greater. It is important to note that of the patients with eclampsia, 11.3% of them were pregnant for the third time or more, and these multiparous patients make up 10.8% of all HELLP patients. This observation indicates that although preeclampsia tends to occur in women pregnant for the first time, the multiparous patients are actually the high-risk group especially prone to progressive complications.

THE RELATIONSHIP BETWEEN PIH AND MULTIPLE GESTATION

It has been observed that women with multiple gestations have a higher probability of developing PIH than singleton pregnancies. Of the women with twin pregnancies, 21%[21] will be diagnosed with PIH. In addition, if twin gestation occurs during first pregnancy, the likelihood of primagravid twin pregnancies to develop

preeclampsia drastically increases to 14 times higher[22] in comparison to multiparous singleton pregnancies. More importantly, besides the elevated frequency of PIH, the severity of its complications whether it is hypertension, proteinuria, or eclampsia, is also much more concerning in twin than in singleton pregnancies[23]. Not unexpectedly, these complications occur at an even higher frequency and more serious conditions in multiple gestations of triplets and greater than in twin pregnancies[24]. According to this study, of all the PIH patients, 286 patients are with twin gestations (6%) and 36 patients are with triplets (0.76%). From the 1995 perinatal annual report, the occurrence of twin gestation is 1.55% and that of triplets is 0.14% in Taipei. It is save to conclude that multiple gestation is indeed a risk factor for PIH. Of the multiple gestation with concurrent preeclampsia cases, 29% of the twin pregnancies eventually developed severe preeclampsia and 1.3% had eclampsia. And of those triplet pregnancies, 36% have severe preeclampsia. From these statistics, it is clear that the likelihood of developing severe preeclampsia is in fact elevated in triplet pregnancies. However, there still lack statistical data to date to confirm that twin gestation with super-imposed PIH will have a more severe course than singleton pregnancies in Taiwan.

THE RELATIONSHIP BETWEEN PIH AND GESTATIONAL AGE

It has been well accepted that PIH rarely occurs prior to 20-weeks gestation. Thus, if hypertension is detected early in pregnancy, it is necessary to suspect that the patient may have chronic hypertension or other medical diseases superimposed with pregnancy. And the earlier the preeclampsia occurs, the more grave the prognosis is for both the mother and the fetus. According to the data collected, PIH diagnosed prior to 32-weeks gestation consisted of 38.9% of all cases. However, for the patients who progressed to severe preeclampsia, a significant 48.6% of them were diagnosed with PIH prior to 32-weeks gestation. And for the patients who had HELLP syndrome, an overwhelming 59.8% were diagnosed with PIH prior to 32-weeks.

THE RELATIONSHIP BETWEEN PIH AND SEASONAL CHANGES

A few literature have suggested that seasonal changes may play a role in the development of preeclampsia[25]. However, other studies from the United States have conflicting results, reporting that such relationship does not exist[26]. Our data indicated that in all the regions under study in Taiwan, the frequency of developing PIH remains relatively constant from January to December. It seems that PIH is independent of seasonal changes.

MATERNAL MORBIDITY AND MORTALITY

PIH MORTALITY

Of all the PIH cases within the recent

five years, only 7 cases resulted in maternal death, with a mortality rate of 0.16%. This percentage is slightly lower than the earlier reported 0.32% by Chen from Ho-Ping Hospital in 1984. Of the above cases, final cause of death are as follows: DIC with sepsis (TriService General Hospital), hypoxic encephalopathy with sepsis (Veterans General Hospital, Taipei), aortic aneurysm rupture (Chung-Gung), ICH with brain edema (Chang-Hua Christian Hospital), and PIH with acute fatty liver (Buddist Tzuchi General Hospital). The cause of death are unknown in two other cases. Of the above cases, IVH, hypoxic encephalopathy, and DIC are the primary cause of death, keeping in mind that sepsis may have played a undeniably significant role as a contributing factor.

PIH MORBIDITY

Of the patients with pregnancy related complications, abruptio placenta represented 4.2% of all cases. The next most common pathology is acute renal failure, which also made up 3.7%, then declining in frequency are postpartum hemorrhage 1.8%, HELLP syndrome 1.8%, pulmonary edema 1.5%, pleural effusion 0.95%, retinal detachment 0.19%, cerebral edema 0.15%, and finally ARDS 0.06%. These complications tend to occur in patients with severe preeclampsia. However, a few patients with mild preeclampsia are still susceptible to such severe complications of PIH, thus they cannot be hastily neglected.

MILD PREECLAMPSIA MORBIDITY

Of the complications which occurred in patients with mild preeclampsia, 57 patients had abruptio placenta, which represented 2.5% of all complications in this group. This is slightly higher than the 1% incident rate reported by other nations[27, 28]. Subsequent complications are listed in the order of decreasing frequency: postpartum hemorrhage 1%, pulmonary edema 0.3%, pleural effusion 0.3%, acute renal failure 0.1%, and retinal detachment 0.1%. In particular, one case which resulted in maternal death was reported, with the cause of death being ruptured aortic artery aneurysm (Chung-Gung). Although the general perception of mild preeclampsia is that it has similar outcomes postpartum as that of normal pregnancies. While this may be the case, it is crucial to note that for patients with cardiovascular diseases, such underlying conditions may lead to serious if not detrimental outcomes when extra precaution is not taken. Furthermore, the frequency of postpartum hemorrhage also tend to be higher in patients with mild preeclampsia (RR=2.35)[29]. Consequently, such these patients deserve detailed, if not meticulous, medical attention.

SEVERE PREECLAMPSIA MORBIDITY

The clinical profile of patients with severe preeclampsia is as follows: 96% of the patients have blood pressure greater than 160/119 mmHg, 74% of the patients has

their 24-hour urine protein greater than 4g. Again, in declining order, other complications include headache in 36% of the patients, oligouria (24-hour urine volume less than 500ml) 19.2%, severe abdominal pain 13%, blurry vision 12.6%, low platelet 9.7%, altered liver function 7.3%, pulmonary edema 4.6%, and DIC 3.7%. It is worth mentioning that a significant number of patients with oligouria were under the care of MacKay Memorial Hospital. This unusually high percentage of oligouria cases (63%) may be contributed by the large number of transferred patients to this hospital. If MacKy Memorial Hospital's data were not included from the analysis, then oliguria substantially decreases down to 6.6%.

MATERNAL COMPLICATIONS

In this category, acute renal failure is the most frequently observed complication (14.1%). Subsequent pathologies in decreasing order are low platelets 9.7%, abruptio placenta 7.6%, ARDS (adult respiratory distress syndrome) 0.5%, and cerebral edema 0.2%. It is clear that the frequencies of these complications are much higher in this category when compared to those patients with mild preeclampsia, yet this is not unexpected. Furthermore, if this data were to be compared with the numbers reported by Chang-Hua Christian Hospital earlier, there exists a substantial increase in acute renal failure, 14.1% vs. 5.7%, while the incidents of abruptio placenta do not vary significantly. When compared with data published by other nations, Taiwan incidence rate for acute renal failure remains much higher, 14.1% vs 0.91 % or 5.0%, respectively[30, 31]. For other complications, their frequencies are lower in Taiwan. The comparison is as follows: abruptio placenta (7.6% vs 21.7%), low platelets (9.7% vs. 20%), and DIC (3.7% vs. 8.3%). It is important to note that for patients with severe preeclampsia, they have a 3.8 times higher chance of developing abruptio placenta than those women with normal pregnant course[32]. Incidentally, severe preeclampsia remains as the primary cause of abruptio placenta. Interestingly, however, the prognosis of these fetuses is similar to that of those cases with abruptio placenta but normal blood pressure[33]. On the other hand, severe preeclampsia has been linked with three cases of maternal death, with the mortality rate of 0.2%.

HELLP SYNDROME MORBIDITY

In order to diagnose HELLP syndrome, three conditions must occur: hemolysis, elevated liver enzymes, and low platelets. However, the debate of HELLP syndrome as an independent disease entity or whether it represents a manifestation of preeclampsia remains disputable. Among patients with HELLP syndrome, near 10% do not have preeclampsia while another 30% of the cases occur postpartum. It is these atypical clinical presentations which make the diagnosis of HELLP difficult[34]. Consequently, it has been

proposed by some to use the term "partial HELLP syndrome" to describe those patients who only meet one or two of the diagnostic criteria[35]. Of the reports published by other nations, the most common complication associated with HELLP syndrome is DIC, 38%. Subsequent morbidities are abruptio placenta 7-20%, acute renal failure 2-8%, and pulmonary edema 4.5-6%. The survey from our study shows that the most frequently observed complication in Taiwan is abruptio placenta 16.9%. Others include pulmonary edema 9.6%, acute renal failure 6.0%, and postpartum hemorrhage 4.8%. These are all similar to the incidences reported by others. In contrast, the recurrence rate of HELLP syndrome remains unclear, ranges between 3% to 27% all have been reported. For patients with HELLP syndrome, they are at an increased risk for premature birth (21%), preeclampsia (19%), IUGR (12%), and abruptio placenta[36]. As for mortality due to HELLP syndrome, death rates between 0.9%[37] to 3.5%[38] have been reported in other nations. However, there were no cases of maternal death in this study, thus such assessment cannot be made.

ECLAMPSIA MORBIDITY

Causes for seizure in patients with eclampsia remain unknown. However, it has been suspected that the primary cause may be related to pathologic changes in the central nervous system. For example, cerebral hypoxia, cerebral hemorrhage, vasospasm, and cerebral edema all have been implicated. And in most cases, there are no warning signs for the development of eclampsia. According to a study published in England, as high as 38% of the eclamptic patients did not have any associated syndromes of preeclampsia. Thus, it has been suggested that the term "preeclampsia" may contribute to the misconception of eclampsia and may cause misunderstanding of its pathogenesis.

Many nations has reported that the occurrence of eclampsia prior to parturition is around 80% (56%-91%). In particular, late-onset eclampsia, which occurs at least 48 hours postpartum, composed of 56% of all postpartum eclampsia cases. According to the statistical data from 1971-1982 published by Chang-Hua Christian Hospital, 67% of eclampsia occurred peripartum while postpartum eclampsia represented 19% and eclampsia during labor, 14%. From this current survey which examined the frequency of eclampsia that occurred peripartum, during labor, or postpartum, their occurrence rates are 73%, 16%, and 11% respectively. It is interesting to note that the late-onset eclampsia occurs at a much lower frequency in Taiwan, in contrast to that reported by other nations (16% vs. 56%). As for maternal complications due to eclampsia, abruptio placenta (12.2%) still remains as the primary cause of morbidity. Other complications include postpartum hemorrhage 6.1%, pulmonary edema 4.3%, acute renal failure 1.7%, and ARDS 0.9%. Data from other countries suggest that maternal

complications incorporate the following: abruptio placenta 4%-16%, pulmonary edema 4%-5.4%, and acute renal failure 1.3%-6.3%.

Interestingly, of all the maternal complications that can be attributed to PIH, cases of subcapsular liver hematoma were not observed. Yet, there were 13 patients with severe preeclampsia who had "severe upper abdominal pain" as a clinical presentation. Such weak association may be due to the tendency for severe preeclamptic and eclamptic patients to have atypical manifestations of their pathology. While the cause of abdominal pain still awaits further investigation, it is unlikely to be a direct consequence of subcapsular hepatic hemotoma. Furthermore, of the patients with severe preeclampsia, 14.1% of them had acquired acute renal failure. This is in discordance with the statistics published by other nations. According to Krane and colleague in 1988[39], acute renal failure is actually a rare complication for patients with preeclampsia; it usually occurs in older women who has had been pregnant before[40]. Since this survey is a preliminary report of PIH statistics for Taiwan, many of the discrepancies addressed above still require additional data and await further investigation.

MODE OF DELIVERY

Termination of pregnancy is the definitive treatment for pregnancy induced hypertension. Especially when complications of PIH severely threaten the well-being of either the mother or the fetus, prompt delivery usually can diminish its death rate. In general, patients with either transient hypertension, chronic hypertension, or mild preeclampsia should not be treated any differently than normal pregnancy when deciding their method of delivery. Such decision making should be based primarily on those routine obstetrical indications for cesarean section and not be influenced by the presence of PIH. According to the foreign literature between 1987 to 1995, no significant differences in fetal outcome was observed for patients with mild preeclampsia who received medication vs those who had not been treated. Similarly, cesarean delivery did not play a role in improving fetal outcome. However, the cesarean section rate ranges between 19% to as high as 43%. In particular, the cesarean rate for preeclamptic patients in Taiwan even reached 54%. When compared to the 42% published by Chang-Hua Christian Hospital earlier, cesarean rate seems to be at an upward trend. This can be partially explained by the consistently higher rate of cesarean section in Taiwan. Even more dramatic is the cesarean rate for preeclamptic patients in People's Republic of China, which is 83%[41]. There had been reports which claims that the success rate for induction tends to be higher in preeclamptic patients. However, most of the recent studies indicate otherwise, that patients with preeclampsia are actually more likely to fail

induction when compared to patients with a normal pregnancy course[42, 43]. This possibly may be a contributing factor for the higher cesarean rate in the PIH patients.

Due to the likelihood of developing severe complications during pregnancy, cesarean section may be an appropriate option to reduce maternal or fetal morbidity for those patients with severe preeclampsia but still preterm, or for those without satisfactory cervical ripening. Consequently, it is not unexpected that for this group of patients, the cesarean section rate is much higher in comparison. Data from Chang-Hua Christian indicate a cesarean rate of 59% during 1987 to 1990. Yet according to our survey the percentage is as high as 74%, with 34% of these patients with failed induction. Further data are necessary in order to investigate the precise indications for these cesarean sections. Since severe preeclampsia itself is not an indication for cesarean section, induction via PGE_2 or oxytocin is appropriate when the patient is mature for labor or is at term, provided that she does not have any contraindications for induction.

Once eclampsia has occurred, termination of pregnancy becomes not only necessary but urgent. And the most speedy method of delivery is via cesarean section. The proportion of cesarean sections in preeclamptic patients in foreign countries is apparently at an upward trend, from Zuspan's report of 1.4% in 1966[44] to Dallas's 23% in 1975[45] to Douglas' 54% in 1994. It seems that rate of cesarean section is not only increasing but also at a rapid rate. Coincidentally, from Chang-Hua Christian's report of the 22% cesarean rate in 1986 to the current 78% section rate noted by this survey, this increase reflects physicians' preference for cesarean section as a means of pregnancy termination in Taiwan as well.

From this survey, it was found that of all the PIH patients who underwent cesarean sections, 13.6% of them had general anesthesia, 61.4% obtained spinal anesthesia, and 25% received epidural anesthesia. In the past it has been well accepted that epidural is the safest method of anesthesia in patients with preeclampsia[46]. However, Wallace and colleagues[47] has suggested that general anesthesia, epidural, or spinal plus epidural anesthesia are all acceptable choices, since no significant differences in maternal or fetal outcome were observed among the three methods.

FETAL OUTCOME

Well-being of the baby is intrinsically associated with and closely dependent on numerous factors such as gestational week at which preeclampsia occurs, gestational age at birth, the severity of preeclampsia, multiple gestations if present, and complications secondary to preeclampsia or other chronic diseases. For those patients with mild preeclampsia, fetus' growth and development are similar and comparable to normal pregnancies. The perinatal death frequency is approximately 1/1000 while

that of intrauterine growth retardation (IUGR) is 4%. Of all the factors that may play a role in fetal outcome, prematurity secondary to preeclampsia has the worst prognosis[48]. Among the newborns less than 37-weeks gestation, the perinatal mortality is 10.5% while IUGR represents 18.2%. Furthermore, twin gestation with super-imposed preeclampsia has a significantly poorer outcome in comparison to singletons; this is especially manifested through the birth weight of the fetus[49]. According to this survey, newborns with birth weight less than 2500g represents 40% of all life births while those weighing less than 1500g made up another 12.6%. As Apgar scores can accurately predict fetal outcome, it was found that 70.5% of the infants had one-minute Apgar score greater than 7, and 9% with Apgar less than 3. Subsequently, 85.1% had five-minute Apgar greater than 7, 4.5% with less than 3. Including all the PIH patients in the analysis, 34.0% were less than 36-weeks gestation, 24.8% had IUGR, and 2.9% resulted in stillbirth. Neonatal mortality is 21/1000. When the severity of pathology is taken into consideration, patients with mild preeclampsia have the following clinical profile: 32.7% with birth weight less than 2500g, 7.3% weighing less than 1500g, 78% with 1-minute Apgar greater than 7 and 4.6% with less than 3, 90% with 5-minute Apgar greater than 7 and 2.6% with less than 3, 23% with less than 36-gestational weeks, 13.2% with IUGR, 1.6% resulted in still birth, and finally the neonatal mortality rate is 7/1000. The statistics for preeclamptic patients from foreign countries are as follows: IUGR from 4%-19% all have been reported, birth weight ranges from 2200g to 2800g, gestational week is between 35 to 38 weeks at delivery, and perinatal death rate varies from 0 to 5.1%. The above numbers are quite similar to the frequencies observed in Taiwan.

When fetal outcome is compared between patients with mild preeclampsia vs those with severe preeclampsia, it is not surprising that the latter has more grave prognosis. The data from National Taiwan University Hospital published in 1989 regarding patients with severe preeclampsia shows: 48.2% were less than 36-weeks gestation, 72% had IUGR, and perinatal mortality was 5.4%. The current survey of severe preeclamptic patients has the following result: 58.2% were less than 2500g at birth, 18.2% were less than 1500g, 10.6% had 1-minute APGAR of less than 3, 6% had 5-minute Apgar less than 3, 53.2% were born at less than 36-weeks in gestation, 30.4% had IUGR, 2.4% resulted in stillbirth, and perinatal mortality was 40/1000. Clearly these statistics reflect poor outcome, although IUGR seems to be at a decline relative to data from 1988. If and when HELLP syndrome develops, the prognosis for the fetus is even more catastrophic. uch dire outcome is manifested through these gloomy statistics: 83.7% weighed less than 2500g at birth, 21.7% were less than 1500g, 38.6% had 1-minute Apgar less than 3,

13.3% with 5-minute Apgar less than 3, 83.1% were born at less than 36-weeks in gestation, 32.5% with IUGR, 6% resulted in stillbirth, and neonatal mortality was 10.8%. Data published by Sibai and colleagues[50] in 1986 for patients with HELLP syndrome also showed similar results: 31.6% of the fetuses were small-for-gestation-age (SGA), 81.6% were born at less than 36-weeks, 19.3 % resulted in stillbirth, and neonatal mortality was as high as 17.4%. Thus, it is intuitively obvious, if not redundant, to point out that the above data confirm that fetal outcome is inversely proportional to the severity of diseases.

Despite the grave statistics, it seems that the frequency of stillbirth is declining in recent years. Such improvement may be attributed to the development of the more sophisticated ultrasound technologies. For example, Doppler may now be used for fetal survillance or for the detection of placental abruption, thus fetal well-being may be more accurately monitored. According this statistical analysis, eclampsia and HELLP syndrome seem to result in similar fetal outcome. Fetuses born to these two groups have the following clinical profile: 26.3% weighed less than 1500g at birth, 20% had 5-minute Apgar of less than 3, 55.7% were less than 36-weeks in gestation, and 31.3% experienced IUGR, 6.1% ended in stillbirth, and neonatal mortality was 10.4%. Similarly, Chang-Hua Christian's report in 1986 showed that only 15.5% of the fetuses were less than 36-weeks gestation, neonatal mortality was 10.2%, stillbirth was 5%, and total perinatal mortality rate was 17.6%. (Table 4)

Undeniably, the severity of pregnancy induced hypertension may be critical in determining fetal outcome. Yet, all of the above are crucial factors which can drastically influence fetal outcome. However, with the advancement of ultrasonography and better fetal surveillance, prematurity may eventually become the primary cause of neonatal mortality and perinatal fatality as a result of preeclampsia.

DISCUSSION

Pregnancy induced hypertension is a major cause of death for both the fetus and the mother alike. Its incidence rate differs greatly, depending on geographical regions. Even in Taiwan, data regarding PIH fluctuates quite significantly and is in need of nation-wide investigation. Thus, this survey, which covers comprehensive statistical information from fourteen major medical centers in Taiwan, can provide valuable and reliable insights. The frequency of preeclampsia and eclampsia in Taiwan is much lower than that reported in other foreign nations. Furthermore, the rate of occurrence and the prognosis for both the mother and fetus do not vary significantly from region to region. Theoretically, this study is targeted toward medical centers and therefore the reported frequency is expected to be higher than the actual prevalence in the general population. According to previous

analysis, the frequency for Asians in the United States to develop preeclampsia is comparable to that of Americans. And for the neighboring nations, China also has an occurrence rate of 16.5%[51]. Thus, race and social habit may not be the major contributing factors for such low percentage observed in the survey. As it is known that there are numerous risk factors for preeclampsia, this survey indeed confirms that parity, maternal age, and multiple gestations are obviously associated with preeclampsia. However, there are also many confounding factors, such as family history, history of preeclampsia during previous pregnancies, urinary tract infections during pregnancy, level of education, prenatal care, obesity, and diabetes mellitus, which showed equivocal results in this study. Thus, their roles as risk factors for preeclampsia still require further elucidation.

The exact cause of pregnancy induced hypertension remains debatable. There are four hypothesis which are more widely endorsed and are currently under rigorous investigation:

1. Placenta Ischemia
2. High serum VLDL concentration causing endothelial cell wall damage.
3. Immunological dysfunction leading to the excess production and secretion of cytokine, proteolytic enzymes, and free radicals. Consequently, trophoblasts and endothelial cells become functionally altered, the end result being the inability for spiral artery to invade the uterus.
4. Hereditary factors, possibly with contribution from both maternal and fetal genetic elements which may simultaneously influence the occurrence of PIH.

The clinical presentation of pregnant induced hypertension is multifaceted. Besides the hypertension, proteinuria, and edema which are the defining symptoms, severe preeclampsia, HELLP syndrome and other atypical manifestations, such as cold-like symptoms or malaise, are also not uncommon[52, 53]. Consequently these presentation can add to diagnostic difficulties. Traditionally, the magnitude of elevated blood pressure has been viewed as a diagnostic indicator and used as a measure of severity. Yet, the measurement of blood pressure and clinical presentations can fluctuate significantly. Often patients may present with edema, proteinuria, hyperlipidemia, or other systemic dysfunction as the primary manifestations of pathology. Thus, Sibai and colleagues proposed a standard method of measuring blood pressure in 1998[54], and addressed factors which may influence the accuracy of measurement: proper instrumentation, cuff size, position of the patients, and resting time prior to measurement. Nevertheless, such ideal procedure may not be practical in Taiwan due to the nature of the its medical system and practice at present time. Nonetheless, besides the meticulous follow up of hypertension, for those patients with normal blood pressure but have proteinuria

and edema, it is especially necessary to beware of other medical complications in these patients.

In general, the occurrence of preeclampsia is under the influence of numerous factors, yet it has been accepted as a preventable complication of pregnancy. In the recent years death rate due to eclampsia has been on the decline in Taiwan. However, from 1995 to 1997, it remains as the number three cause of death in pregnant women, only ranking behind postpartum hemorrhage and amniotic embolism. As for maternal complication, preeclampsia and eclampsia rarely cause permanent systemic dysfunction. Even for patients who developed acute renal failure, most do recover and seldom need hemodialysis. Although statistics from this survey does indicate that the proportion of acute renal failure tend to be on higher, this may be related to the definition of disease diagnosis. Although fetal lung does mature at an earlier stage for PIH patients, fetal outcome still primarily is a function of gestational age. Note that steroids may stimulate lung maturation. Otherwise, abruptio placenta is another major cause of fetal demise. Unfortunately the detection or the prediction of abruptio placenta still remains difficult. As a result, emphasis is placed on fetal surveillance, such as fetal heart beat and Doppler sonographic examination of fetal circulation. Even though mode of delivery seems not to have a direct consequence on fetal outcome, under the pressure of frequent medical suits, cesarean section rate remains high and may continue to be elevated. Currently the proper method of anesthesia is debatable. It has been proposed that as long as the monitoring of maternal hemodynamics can be sufficiently achieved, even spinal anesthesia can be applied.

Hypertension itself is a complicated systemic disease which affects the entire body organs. However, there are still questions from its cause, mechanism, and pathology to clinical prediction, prevention, and intervention which all await elucidation. This report thus represents only an introductory analysis of current states of pregnancy induced hypertension in Taiwan, with further comparison between various nations. Besides establishing a more comprehensive data regarding PIH in Taiwan, hopefully that by comparing statistics with foreign countries this study will also stimulate further interests for future investigations. Especially for the topics not addressed in this survey and the controversies not resolved in this analysis, perhaps this report will serve as the beginning to a more far reaching and thought provoking study.

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台灣之妊娠高血壓

前言

妊娠高血壓是人類獨有的疾病，也是孕期中常見的合併症之一。與出血、感染三者同為造成孕婦死亡的主因[1]。在美國是孕婦死亡的第二大原因[2]，僅次於產後出血。在台灣地區，隨著出血與感染造成產婦死亡率的降低，妊娠高血壓所造成產婦死亡的比例逐漸上升。1974 到 1985 年間，妊娠高血壓佔了產婦死亡原因的 23.7%[3]，僅次於出血死亡的 42.4%。造成產婦高血壓的原因，至今仍無定論。目前較能被接受的，可能與早期懷孕時，母體的免疫系統或其他原因使胎兒滋養層（trophoblast）細胞無法侵入子宮有關[4]。由於妊娠高血壓的復發率很高，讓人聯想到它與基因的關係。的確也有一些可能的基因被發現，包括 HLA-DR4[5]，Angiotensinogen[6]的基因，甚至粒腺體中的 DNA[7]都可能扮演一部份致病的角色。這些發現似乎意味著在受精卵結合的那一剎那，就註定了疾病的發生。除了這些免疫、基因的因素外，影響妊娠高血壓發生率的因素，還包括年齡、胎次、種族[8,9]、生活習慣（如吸煙等）、營養[10]、荷爾蒙等[11]。因此發生率也隨族群的不同而有明顯的差異，從 3%到 10%[12]都曾有人報告過。若不考慮這些因素，則發生率約在 5%左右。台灣本土報告的差異性也很大，根據彰基在不同年代的報告，發生率從 9.4%[13]到 1.8%不等。由於國內近年缺乏大規模關於妊娠高血壓的報告，所以我們蒐集了全省 14 家醫學中心從 1993 年到 1997 年中發生妊娠高血壓的案例加以分析，希望能藉此描繪出台灣本土近五年來的概況。

流行病學

發生率

妊娠高血壓（Pregnancy induced hypertension, PIH）是一種通稱，泛指懷孕期間新出現，或是因懷孕而加重的高血壓。因此在分類上可再分為 Transient hypertension, Chronic hypertension superimposed preeclampsia, preeclampsia eclampsia。這次的分析中，台灣北、中、南、花東地區 14 家醫學中心在五年中的生產人數共有 206551 人次，PIH 發生率為 2.3%，這其中還包括了 Transient

hypertension,及 Chronic hypertension superimposed preeclampsia 的 650 位案例。其發生率分別為 0.4%及 0.14%。扣除這些案例，則 preeclampsia 的發生率為 2.06%，這與國外平均 5%的發生率而言顯然是低了許多。其中北部地區的醫學中心發生率為 2%，中部地區為 3.2%，南部地區為 2.8%，花東地區（慈濟醫院）發生率則為 2.3%。這可能與中部地區醫院的數目及轉診的人數有關。

在子癲前症的患者中， 輕度子癲前症佔 58.9%，重度子癲前症佔 38.4%。其中有 2%有發生 HELLP 症候群。子癲症則佔了 2.7%。若以全部生產人數來看發生率，輕度子癲前症的發生率為 1.1%，重度子癲前症為 0.7%。HELLP 症候群為 0.4/1000，子癲症的機率為 0.5/1000。彰化基督教醫院在 1986 年的報告中，子癲症的發生率為 0.15/1000，在子癲前症的患者中，HELLP 症候群發生率為 11%。國內從 1972 年到 1981 年間，子癲症的發生率從 1974 年最高的 4/1000 逐年下降。到 1981 年 1/1000 左右。若與英國比較，子癲症在全部產婦的發生率從 1930 年 7.4/1000，到 1994 年 0.49/1000 [14]，也是逐年遞減。開發中國家的比例較高，巴基斯坦 2.14% [15]，土耳其 7.71% [16]。由於子癲症的危險因子包括年齡、經產婦與是否接受產前照護有關 [17]，因此，子癲症比例下降間接地表示了國內周產期醫療水準的進步。

PIH 與年齡、胎次的關係

妊娠高血壓好發於高齡產婦及初產婦。Spellacy 在 1986 年就報告 40 歲以上產婦發生妊娠高血壓的機會是 20 到 30 歲孕婦的三倍。Loug PA [18] 在 1979 年以及 Sibai BM [19] 等人在 1995 的報告都指出初次懷孕得到 PIH 的機會較高，甚至 60%的患者都是初產婦。利用多變數分析來評估 PIH 的危險因子，則高齡與初次懷孕都是 PIH 的高危險群。有趣的是，大多數的高齡產婦都是經產婦，而高齡經產婦發生妊娠高血壓的機會仍然是年輕孕婦的 2.7 倍 [20]。

在這次台灣地區，妊娠高血壓患者中，30 歲以上的孕婦佔了 55.4%，35 歲的孕婦佔了 23.1%。在產次分佈上，初產婦佔了 55.8%，第 4 次或第 4 次以上懷孕則佔了 8.1%。根據 1999 年婦幼衛生研究所的"婦幼衛生之主要統計"，86 年度台灣生育胎次中，年齡大於 30 歲的佔所有產婦的 30%。而大於 35 歲的只佔 6.2%，初產婦則佔 42.39%，多胎經產婦（曾有三次或三次以上生產經驗）佔 4%。由此可看出年齡、胎次與妊娠高血壓的關係。

若按疾病嚴重程度加以分類，在輕度子癇前症的患者中，35 歲以上佔 18.5%，產次分佈中，初產婦佔 67.3%。重度子癇前症患者 35 歲以上佔 26.8%，初產婦佔 51.4%。HELLP 症候群中，35 歲以上佔 19.2%，初產婦佔 44.6%。子癇前症患者中，35 歲以上佔 24.4%。值得注意的是，子癇症中曾有 3 次或 3 次以上生產經驗的產婦佔了 11.3%，HELLP 症候群患者中，則佔了 10.8%。這顯示出雖然子癇前症好發於初產婦，但多胎經產婦反而是發生合併症的高危險群。

妊娠高血壓與多胞胎的關係

多胞胎孕婦發生子癇前症的機會比單胎懷孕要高（RR=6.0），在懷雙胞胎的婦女中有 21%會發生妊娠高血壓 [21]。若與單胎經產婦比較，則雙胎初產婦發生子癇前症的機會增加了 14 倍 [22]。除發生率增加外，雙胞胎孕婦發生子癇前症的程度也比單胞胎要嚴重，不論是高血壓、蛋白尿或是發生子癇前症的機會 [23]。在三胞胎或多胞胎妊娠時，發生子癇前症的機會比雙胞胎又更高。其嚴重性也比雙胞胎妊娠更甚 [24]。在這次的分析資料中，所有妊娠高血壓的病患中，有 286 位是雙胞胎（佔 6%），36 位（0.76%）是三胞胎。根據 1995 年周產期醫學會白皮書統計，北市雙胞胎發生率為 1.55%，三胞胎發生率 0.14%。相較之下不難看出多胎妊娠的確是妊娠高血壓的高危險群。在多胞胎妊娠合併子癇前症的患者中，有 29%的雙胞胎發生重度子癇前症，有 1.3%的雙胞胎發生子癇症。三胞胎孕婦中，有 36%是重度子癇前症。單就這些數字而言，三胞胎發生重度子癇前症的機會的確偏高。但是在程度上，並沒有任何資料可以證實國內雙胞胎合併妊娠高血壓的嚴重性會大於單胎懷孕的婦女。

妊娠高血壓與妊娠週數的關係

妊娠高血壓很少發生在 20 週以前，若早期懷孕就發現高血壓的話，通常會懷疑孕婦是否合併有原發性高血壓或是其他內科合併症。子癇前症發生的週數越早，胎兒或母親的癒後越差。在國內的資料中，於 32 週前被診斷妊娠高血壓者佔了 38.9%，但是在重度子癇前症的患者中，有 48.6%在 32 週前就被診斷有妊娠高血壓、HELLP 症候群患者有 59.8%在 32 週前被診斷出有妊娠高血壓。

妊娠高血壓與季節的關係

少數文獻曾提及氣候的改變與子癇前症的發生有關 [25]。但在美洲地區的報

告則沒有這個現象[26]。這次的資料顯示全國不論在北、中、南或是花東地區，1到12月發生妊娠高血壓的機率都類似，並沒有任何明顯的相關性。

產婦罹病率及死亡率

死亡率

在五年內所有妊娠高血壓的案例中，共有 7 例死亡，死亡率為 0.16%。與和平醫院 1975 年到 1984 年報告的 0.32%稍低。5 位死亡病例的原因包括了 DIC with sepsis(三總), hypoxic encephalopathy with sepsis(北榮), aortic aneurysm rupture(長庚), Intraventricular hemorrhage with brain edema(彰基), acute fatty liver(慈濟)。另有兩病例未註明原因。其中顱內出血及缺氧，以及 DIC 仍是造成死亡的主因。但是菌血症可能也扮演著相當重要的角色。

妊娠高血壓罹病率

就全部患者的罹病率 (morbidity) 來看，發生胎盤早期剝離的佔了 4.2%，其次是急性腎衰竭，佔了 3.7%、產後出血 1.8%，HELLP 症候群 1.8%、肺水腫 1.5%，肋膜腔積水 0.95%，視網膜剝離 0.19%，大腦水腫 0.15%，及 ARDS0.06%，這些合併症的主要發生於重度子癲前症病人。但輕度子癲前症患者仍有少數患者會發生較嚴重的合併症，這是不容忽視的。

輕度子癲前症

輕度子癲前症患者的罹病率中，胎盤早期剝離有 57 人，佔 2.5%。與國外報告的 1%似乎稍微高了些[27, 28]。其次的產後出血 1%，肺水腫 0.3%，肋膜積水 0.3%，急性腎衰竭 0.1%，視網膜剝離 0.1%。其中有一例死亡病例是因為主動脈血管破裂致死（長庚）。雖然一般都認為輕度子癲前症的預後與正常懷孕的產婦預後相似。但是對於有心臟血管疾病的孕婦，它仍可能導致嚴重的後果。此外，輕度子癲前症患者產後出血的危險性也偏高（RR=2.35）[29]，這也是在處理病患時要注意的。

重度子癲前症

重度子癲前症的臨床表現中，有 96%患者血壓大於 160/110mmhg，74%患者 24 小時蛋白尿大於 4g。其次是頭痛 36%、少尿（24 小時尿量少於 500ml）

19.2%，嚴重的上腹痛 13%，視力模糊 12.6%，血小板低下 9.7%，肝功能改變 7.3%，肺水腫 4.36%，DIC3.7%。其中少尿的病患以馬偕醫院報告的比例較高（63%）。可能與轉診的病患數目有關。若去掉馬偕的病例，則比例降至 6.6%。

在母親的罹病率中，發生急性腎衰竭的比例最高，佔 14.1%。其次為血小板數目減少 9.7%，胎盤早期剝離 7.6%，肺水腫 4.0%，產後出血 3.5%，肋膜積水 3.5%，視網膜剝離 0.5%，ARDS0.5%，大腦水腫 0.2%。這些合併症的發生率明顯地比輕度子癲前症要高出許多。若與早期彰基的報告相比較，急性腎衰竭的比例增加許多（141% vs 5.7%）。其他胎盤早期剝離等，則沒有明顯的改變。與國外資料相比，我們急性腎衰竭仍是偏高（14.1% vs 0.91-5.0%）[30, 31]，胎盤早期剝離（7.6% vs 21.7%），血小板減少（9.7% vs 20%）及 DIC（3.7% vs 8.3%）的發生率較低。重度子癲前症患者發生胎盤早期剝離的機會是正常孕婦的 3.8 倍 [32]，也是造成胎盤早期剝離最主要的原因。但是胎兒的預後是與血壓正常的早期胎盤剝離是相似的 [33]。重度子癲前症造成的產婦死亡有三例，，死亡率為 0.2%。

HELLP 症候群

HELLP 包含三個診斷要件：溶血、肝指數上升及血小板下降。它是獨立發生的疾病，還是子癲前症的另一種表現形式，至今仍有爭論。有百分之十的 HELLP 症候群的患者沒有子癲前症的症狀。另外有 30%是發生在產後。這些非典型的表現使診斷變得困難 [34]。甚至有人建議使用"partial HELLP syndrome"來定義那些只發生診斷要件中一項至兩項合併症的病患 [35]。國外的報告中，HELLP 症候群造成母親的併發症以 DIC 的機會最高（38%），其次為胎盤早期剝離（7-20%），急性腎衰竭（2-8%），肺水腫（5-6%）。國內的資料中以胎盤早期剝離最多（16.9%），其次為肺水腫（9.6%），急性腎衰竭（6.0%），產後出血（4.8%），與國外的報告相似。HELLP 症候群患者的再發率從 3%到 27%都有報告。患者下胎發生早產（21%），子癲前症（19%），IUGR（12%）及胎盤早期剝離的機會均會增加 [36]。死亡率方面，國外的文獻報告母體死亡率在 0.9% [37] 到 3.5%之間 [38]。本文統計的資料中並沒有死亡的案例。

子癇症

子癲前症的病患何以會發生痙攣，目前仍不清楚。但是主要原因可能仍是

中樞神經系統的病變，像是大腦缺氧、出血、血管痙攣、大腦水腫等。通常子癲症發生前並不會有先驅症狀。在英國的報告中，有 38%的子癲症患者，在痙攣前並沒有合併子癲前症。因此它們認為「子癲前症」這個名詞可能造成一般人對這個疾病的誤解。

在國外的報告中，子癲症痙攣發生於產前的約佔 80%（56%--91%）。其中遲發型產後痙攣（生產 48 小時後發生）佔了產後子癲症的 56%。彰基統計 1971 到 1982 的報告中，產前痙攣佔 67%，其次為產後痙攣（19%），生產時發生痙攣（14%）。在本次的統計中，產前、產中、產後發生子癲症的機率分別為 73%、16%、11%。其中遲發性子癲症佔了產後子癲症的 16.7%。這個比例與國外報告有些差異。在母體的罹病率中，胎盤剝離仍居首位（12.2%），其次為產後出血（6.1%），肺水腫（4.3%），急性腎衰竭（1.7%），ARDS（0.9%）。

在所有妊娠高血壓造成的母體合併症中並沒有肝臟血腫（subcapscular liver hematoma）的案例，但是在臨床表現上，重度子癲前症的患者中有 13%有嚴重上腹疼痛的表現。這可能與重度子癲前症及子癲症常會表現出非典型的症狀有關。至於其疼痛的原因，可能需要進一步的研究，可能與肝臟血腫沒有直接的關係。另外在重度子癲前症的患者中有 14.1%的急性甚衰竭發生，這與國外的報告相異極大，krane [39] 等人在 1988 年的報告中，急性腎衰竭在子癲前症是屬於少見的併發症，而且常發生於年齡較大的經產婦身上 [40]。國內這份初步報告需要更多的資料才能作進一步的分析。

生產方式

終止妊娠是治療妊娠高血壓最有效的方法。尤其對於瀕臨危險的母親或胎兒，生產常常可以降低其死亡率。一般而言，暫時性高血壓、慢性高血壓以及輕度子癲前症的生產方式與正常妊娠婦女的生產沒有差別，完全以產科的適應症決定是否剖腹生產。國外從 1987 到 1995 年間的報告中，對輕度子癲前症患者給予降血壓藥物與否，與剖腹產率及胎兒的癒後並無差異。其剖腹產率約為 19%到 43%之間。國內輕度子癲前症患者的剖腹產率是 54%，與彰基早期報告的 42%比較似乎有增加的趨勢。可能與國內的剖腹產率一直都偏高有關。中國大陸所有子癲前症患者的剖腹產率更高達 83% [41]。過去曾有報告認為子癲前症患者引產的成功率較高。但是現在許多文獻反而認為子癲前症患者引產成功率

比正常妊娠的婦女要低[42,43]。這也許是剖腹產率居高不下的原因之一。

由於在待產中常發生嚴重的合併症，重度子癇前症的患者若離足月尚久，或是子宮頸成熟度不夠，選擇剖腹生產是減少胎兒及母親合併症的方法之一。所以這類病人剖腹產的比例很高。彰基的報告（1987-1990），剖腹產率為 59%。本文的資料中則高達 74%，其中有 34%患者曾經接受引產。至於這些剖腹產的適應症為何，則需要進一步的資料。重度子癇前症本身並非是剖腹生產的適應症，若病患本身已經有產兆，或是已足月，也沒有引產的禁忌，則使用 PGE2 或是 Oxytocin 都是可行的引產方式。

子癇症一旦發生，即意味著必須要盡快終止妊娠。當然最快的方式即是剖腹生產。國外子癇症剖腹生產率從 1966 年 Zuspan [44] 的 1.4%，1975 年 Dallas [45] 的 23%，到 1994 年 Douglas 的 54%，似乎有一直上升的趨勢。在 1986 年彰基報告的 22%的剖腹產率，到這次資料 78%的剖腹產率，顯示國內也逐漸偏好選擇剖腹產來終止妊娠。

在麻醉的選擇上，所有採剖腹產的妊娠高血壓患者中約有 13.6%接受全身麻醉，61.4%上 spinal anesthesia，25%使用 epidural anesthesia。過去認為 epidural anesthesia 是對妊娠高血壓最安全的麻醉方式[46]。但是 Wallace 等人[47]則認為使用全身麻醉、epidural 或是 spinal+ epidural ，三者對母體及胎兒預後並沒有任何差異。

胎兒預後

胎兒的預後與妊娠高血壓發生的週數、生產週數、疾病嚴重程度、多胎妊娠以及妊娠合併其他的內科疾病有關。在輕度子癇前症的患者其胎兒子宮內生長遲滯與一般的孕婦是相似的。其週產期死亡率約為 1/1000，子宮內生長遲滯約 4%。在所有影響胎兒癒後的因素中，因子癇前症而造成的早產胎兒預後最差[48]。小於 37 週的新生兒中，週產期死亡率為 10.5%，子宮內生長遲滯有 18.2%。此外，懷有雙胞胎的孕婦若罹患子癇前症，其預後也比單胎孕婦要差。尤其在出生體重上，可以看出明顯的差異[49]。在本文的資料，所有所有妊娠高血壓患者的新生兒中，體重小於 1500 公克的佔了 12.6%。第一分鐘 Apgar score 小於 3 的佔 9%，第 5 分鐘 Apgar score 小於 3 的佔 4.5%。生產週數小於 36 週的佔 34%，，子宮內生長遲滯佔 24.8%，死胎（stillbirth）佔 2.9%，新生兒死亡（ neonatal

mortality）為 21/1000。若按疾病嚴重的程度加以區分，在輕度子癇前症的患者中，體重小於中小於 1500 公克者佔了 7.3%。第一分鐘 Apgar scor 小於 3 的佔了 4.6%，第五分鐘小於 3 的佔 2.6%。生產週數小於 36 週的佔 23%，子宮內生長遲滯的佔 13.2%，死胎 1.6%，新生兒死亡率 7/1000。國外報告中輕度子癇前症發生子宮內生長遲滯的比率從 4% 到 19%都有。平均新生兒體重約從 2200 到 2800 公克左右，出生週數平均在 35 週到 38 週之間。週產期死亡率從 0 到 5.1% 都有人報告。國內報告與國外的資料並沒有明顯的差異。相較於輕度子癇前症，重度子癇前症的胎兒預後要差了許多。台大醫院 1989 年的報告中小於 36 週出生的有 48.2%，IUGR27%，週產期死亡率 5.4%。本文資料中新生兒體重小於 1500 公克佔 18.2%。第一分鐘 Apgar score 小於 3 的佔 10.6%，第 5 分小於 3 的佔 6%。出生週數小於 36 週的佔 53.2%，，子宮內生長遲滯有 30.4%，死胎 2.4%，新生兒死亡率 4%。其中 IUGR 的比例似乎有下降的趨勢。若病程進展到了 HELLP 症候群，則胎兒的癒預後更差。出生體重 2500 公克以下就佔了 83.7%，1000 公克以下佔 21.7%。出生週數小於 36 週佔 83.1%，IUGR 的機會 32.5%，死胎 6%，新生兒死亡率 10.8%。由上面的資料可以發現胎兒的預後與疾病的嚴重性成反比。Sibai [50] 等人在 1986 年報告 HELLP 症候群的結果中，SGA 佔 31.6%，小於 36 週初生的佔 81.6%，死產 19.3%，新生兒死亡率 17.4%。相較之下，這幾年中似乎死產的機率減少了，可能與胎兒監視系統及產科超音波的發展有關。利用 Doppler sonogram 可以測量胎盤或胎兒的血流狀況以減少死胎的發生。在本次統計中，子癇症胎兒預後與 HELLP 症候群患者相似，體重小於 1500 公克佔了 26.3%，第 5 分鐘 Apgar score，小於 3 者佔了 20%。出生週數小於 36 週者佔 55.7%。子宮內生長生長遲滯 31.3%，死產 6.1%，新生兒死亡率 10.3%，彰基在 1986 年的報告子癇症患者中只有 15.5%新生兒出生週數小於 38 週，，新生兒死亡率 10.2%，死胎 5%，全部週產期死亡率為 17.6%。

整體而言，胎兒的預後除了前述的危險因子之外，應該與妊娠高血壓本身的嚴重度有關。但是早產仍是子癇前症造成新生兒死亡的主要原因。

討論

妊娠高血壓是造成新生兒及孕婦死亡的重要原因，它的發生率隨著地區不同而有很大的差異。台灣本土資料的差異性也很大，且缺乏全國性的調查。因

此，這次全省十四家教學中心大規模統計的結果，應是比較可信的資料。就發生率來看，台灣子癲前症及子癲症的發生率比國外報告低很多。而且南北與花東地區不論在發生率及母體、胎兒的癒後都沒有明顯的差異。理論上這次蒐集的是一個以醫學中心為背景的資料，其發生率應該比實際的發生率高。根據文獻，亞洲人在美洲發生子癲前症的機會與當地人相似，而鄰近的中國大陸發生率為 16.5% [51]。因此種族與生活習慣，應該不是造成台灣地區發生率偏低的主因。子癲前症的危險因子很多，這次國內的資料，可以看出胎次、年齡、多胞妊娠、與子癲前症有明顯的關連性。但是其它的危險因子，例如家族史、前胎有子癲前症、妊娠期間泌尿道感染、教育程度、接受產檢與否、肥胖、糖尿病患者等，在這次的統計中並沒有呈現出來，值得作進一步的研究。

妊娠高血壓的原因，至今仍不清楚。目前有四種可能的假說被廣泛的研究中：一、胎盤缺氧（placenta ischemia）二、極低密度脂蛋白（VLDL）在孕婦血中濃度增加造成的毒性。三、免疫反應異常，蛻膜（decidua）分泌過量的細胞素（cytokine）、蛋白溶解酵素（proteolytic enzymes）及自由基（free radical）使滋養層細胞及血管內皮細胞功能改變，進而導致螺旋狀動脈（spiral artery）無法侵入子宮。四、基因，可能包括母親與胎兒的基因，共同影響妊娠高血壓的發生。這些主題在台灣發表的文獻中，尚不多見。應該是未來可發展的方向之一。

妊娠高血壓所表現的臨床症狀是很多變的，除了定義中的高血壓、蛋白尿及水腫之外，重度子癲前症、HELLP 症候群，常會出現一些非典型的症狀 [52, 53]。包括全身不適（malaise）及類似感冒般的症狀。這些表現有時會造成診斷上的困擾。傳統上我們都以血壓上升作為診斷的依據及嚴重度的參考。但是在臨床上，常有病患是以水腫、蛋白尿、凝血異常、器官功能喪失為最早出現的症狀。其次，血壓的測量也有很大的變異性。因此，Sibai [54] 等人在 1988 年即提出標準的血壓測量方法，包括：儀器、cuff 寬度、病患姿勢、測量前的休息時間等。以目前國內的醫療環境而言，要依照這個標準來作，似乎可行性不高。至於血壓不高而有蛋白尿、水腫的病患，也要特別小心是否出現其他併發症。

一般而言，子癲前症的發生與否，是由許多因子共同決定的。但子癲症則被認為是一種可以預防的合併症。國內這幾年來子癲前症---子癲症造成的死亡率有逐年減少的趨勢。但是從 95 年到 97 年，它的死亡人數仍居產婦死亡率的

第三名，僅次於產後出血與羊水栓塞。至於母體的罹病率，子癇前症及子癇症很少造成永久性的器官功能障礙，即使發生急性腎衰竭，在產後腎臟功能也大多能恢復正常，很少需要作血液透析。但是在本文統計的資料中，急性腎衰竭的比例偏高，其原因可能與診斷的定義有關。至於胎兒的預後，主要還是決定於生產週數。妊娠高血壓患者的胎兒，其肺部可能會較早成熟。此外，corticosteroid也可用於促進胎兒肺部的成熟，預防胎兒發生呼吸窘迫。胎盤早期剝離，也是胎兒死亡的重要原因，目前並無很好的方法可以預測胎盤剝離的發生。因此加強胎兒的監視、包括胎心速率、及都卜勒超音波檢測胎兒血流都是可行的方法之一。生產方式與胎兒的預後並無明顯的關連性，但是在醫療糾紛的壓力下，剖腹生產比率可能仍會高居不下。至於麻醉方式，目前有人認為，在沒有凝血問題的前提下，只要能監測母親血液動力學的情況，使用 spinal anesthesia 也並非是禁忌。

妊娠高血壓是一種複雜的全身性疾病，它的致病原因、機轉、病理乃至於臨床上的預測、預防與治療，仍存在許多未知。本文僅對台灣目前的妊娠高血壓做一初步的分析，並與國內外的資料相比較。除了建立本土的資料以外，也希望藉由交叉比對中發現與國外的差異，以作為進一步研究的參考。對於文中沒有討論的問題還需要進一步的資料與研究才能得到答案。希望不久的將來能見到更大規模及前瞻性的研究出現。

表 1、 1993 到 1997 年全省 14 家教學中心 PIH 病患特性分佈及胎兒預後

* ()中為百分比，分母為總 PIH 人數。

** 數字即為百分比。

"-" 表示資料不全

	台大	北榮	林口長庚	北長庚	馬偕	北市婦幼	三總	中榮	彰基	中國	中山	高榮	高醫	慈濟	總計
Total delivery	17239	11967	29095	25868	27932	17901	6861	7538	22713	12493	12459	4713	5349	4423	206551
Preeclampsia*	1.9%	2.5%	0.9%	1.4%	3.4%	0.8%	1.4%	5.0%	1.7%	4.9%	0.9%	1.7%	2.9%	2.3%	2.06%
Mild	244(74)	144(37)	137(43)	301(74)	651(62)	78(37)	50(44)	289(53)	236(57)	278(40)	63(58)	17(20)	61(31)	42(41)	58.9%
Severe	80(24)	149(39)	105(33)	45(11)	277(26)	54(25)	37(32)	83(15)	148(36)	305(44)	41(38)	63(72)	87(44)	56(56)	38.4%
Eclampsia	7(2.1)	8(2.1)	14(4.4)	14(3.5)	17(1.6)	3(1.4)	6(5.2)	8(1.5)	9(2.2)	31(4.5)	3(2.9)	2(2.3)	7(3.6)	3(3)	2.7%
Parity(%)**															
=0	36.4	35.2	-	57.1	93.6	26.7	46.9	52.0	59.4	34.7	13.0	43.7	53.6	53.0	55.8%
=1-2	54.2	57.1	-	34.7	6.2	63.1	47.8	29.2	35.4	59.1	75	52.9	40.3	40.9	36.1%
≧3	9.4	7.7	-	8.1	0.19	10.2	5.3	18.8	5.1	6.2	12	3.4	6.1	6.1	8.1%
Age(%)**															
<20	0.6	0.3	0.7	0.5	0.5	1.9	0.0	4.2	2.7	1.2	1.8	2.3	2.0	5.8	
20-34	67.5	66.0	77.9	78.63	85.9	80.8	73.0	76.2	84.2	60.7	80.6	73.6	70.9	76.8	
≧35	31.8	33.7	21.3	20.84	13.6	17.4	27.0	19.6	13.1	6.5	17.6	24.1	27.0	17.4	23.1%
C/S rate(%)**	83.3	46.5	-	83.25	46.5	86.1	76.34	-	77.8	35.2	87.1	89.0	80.1	-	74%
Fetus outcome(%)**															
Birth weight<1500	19.7	14.3	22.9	13.5	9.3	8.0	6.3	11.9	9.4	8.1	11.7	16.7	21.2	14.9	12.6%
Preterm	49.3	34.6	52.1	30.6	34.0	15.6	32.1	26.4	17.4	31.7	20.7	46.9	37.8	-	34%
IUGR	31.3	13.1	19.0	33.25	20.2	30.2	18.8	12.1	7.6	10.8	10.8	29.2	20.7	61.2	24.8%
Stillbirth	4.9	3.4	4.9	1.58	4.6	1.4	0.9	2.0	0.5	0.0	0.9	3.13	6.74	1.5	2.9%
Neonatal mortality	-	2.2	2.5	3.43	1.3	0.0	0.9	0.18	0.9	5.32	1.8	6.23	1.0	6.0	2.1%

表 2、 重度子癲前症的臨床表現

1. Systolic Bp≧160 mmHg or diastolic Bp≧110 mmHg	96%
2. proteinuria (>4g/24hr or persistent 2+)	74%
3. Headache	36%
4. Oligouria	19.2%
5. Severe epigastric pain	13%
6. Visual disturbance	12.6%
7. Thrombocytopenia	9.7%
8. Impaired liver function	7.3%
9. Pulmonary edema	4.6%
10. DIC	3.7%

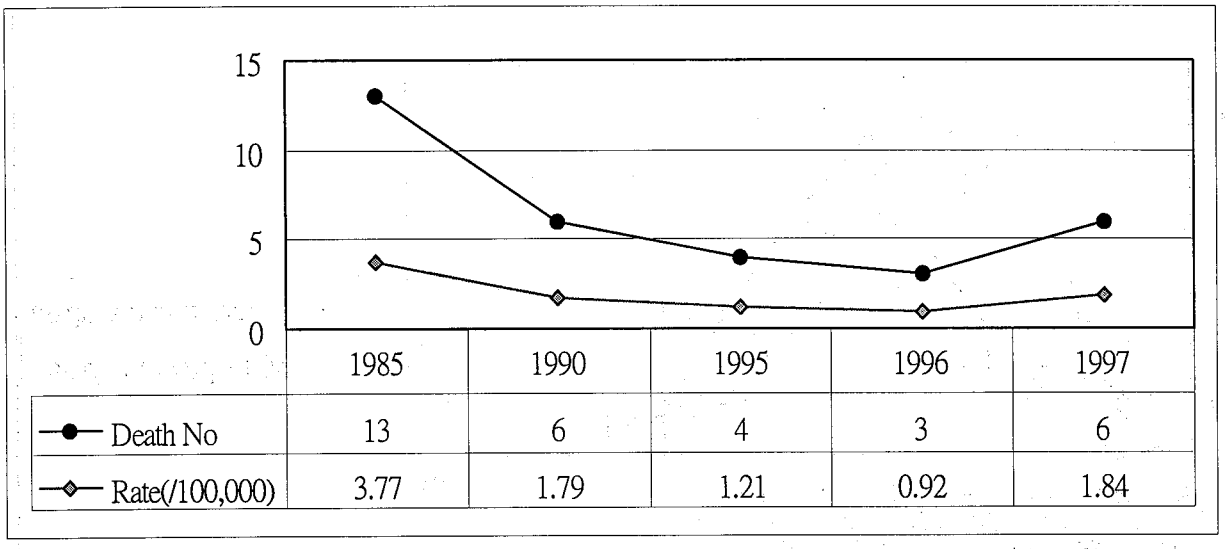
表 3、 子癲前症及子癲症造成孕婦的合併症

	Mild preeclampsia	Severe preeclampsia	eclampsia
Abruptio placenta	2.5%	7.6%	12.2%
Acute renal failure	0.1%	14.1%	1.7%
Pulmonary edema	0.3%	4.0%	4.5%
PPH	1.0%	3.5%	6.1%
Pleural effusion	0.3%	2.6%	1.7%
Retina detachment	0.1%	0.5%	0%
ARDS	0%	0.5%	0.9%
Cerebral edema	0%	0.2%	1.7%
Subcapsular liver hematoma	0%	0%	0%

表 4、 子癲前症及子癲症對胎兒預後的影響

	Mild preeclampsia	Severe preeclampsia	eclampsia
Preterm delivery	23.0%	53.2%	55.7%
IUGR	13.2%	30.4%	31.3%
Stillbirth	1.6%	2.4%	6.1%
Neonatal mortality	0.7%	4.0%	10.4%

圖 1、 1985 到 1997 年間台灣地區 Preeclampsia-eclampsia 的死亡人數及母體死亡率。



	1985	1990	1995	1996	1997
Death No	13	6	4	3	6
Rate(/100,000)	3.77	1.79	1.21	0.92	1.84

圖 2、 輕度及重度子癲前症患者的年齡分佈。

*1997 全年度台灣地區產婦之年齡分佈

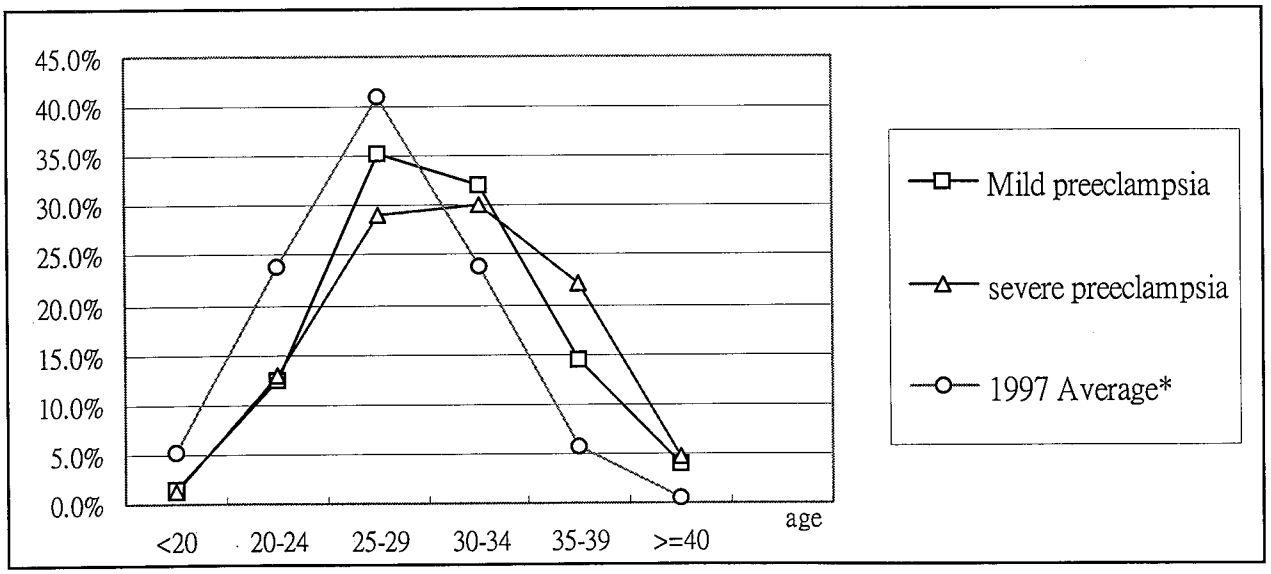
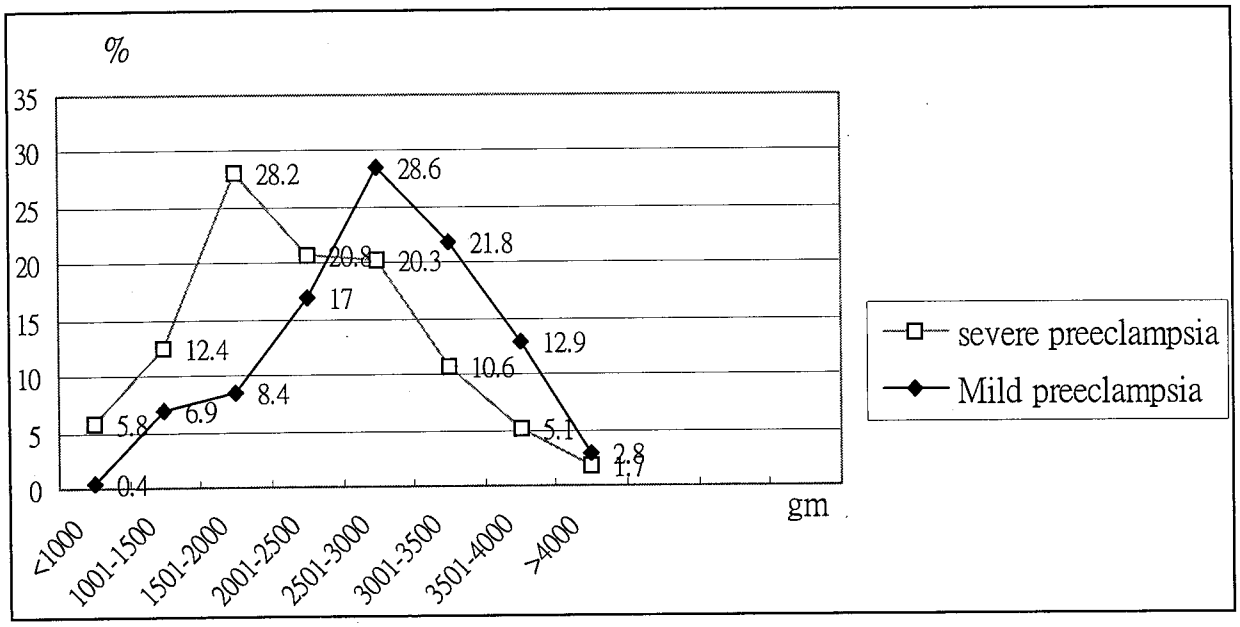


圖 3、1993 到 1997 年台灣地區重度子癇前症與輕度子癇前症患者新生兒出生體重分佈圖



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